PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/000319	06.01.2005	06.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07D487/04, A61K31/53, A61K31/519

Applicant
TAISHO PHARMACEUTICAL CO., LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Von Daacke, A Telephone No. +49 89 2399-8286

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/000319

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/000319

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report
D1: WO 98/35967 A (NEUROCRINE BIOSCIENCES, INC; MCCARTHY, JAMES, R) 20 August 1998 (1998-08-20)
D2: WO 98/08847 A (PFIZER INC; CHEN, YUHPYNG, LIANG) 5 March 1998 (1998-03-05)
D3: EP-A-0 729 758 (PFIZER INC) 4 September 1996 (1996-09-04)
have been considered for the examination procedure.

2. NOVELTY

The claimed subject-matter is considered to be novel (Article 33(2) PCT). The essential structural difference between the claimed compounds and those of D1 relates in the presence of the carbamoyl group.

3. INVENTIVE STEP

The claimed subject-matter does not fulfil the requirements of Article 33(3) PCT for the following reasons.

The closest state of the art for the present application is represented by D1. D1 discloses structurally similar pyrrolopyrimidine and -triazine compounds having CRF receptor antagonistic properties which do not fall under the present application because of the absence of the said carbamoyl group. In the present application, such a structural variation is alleged to lead to pyrrolopyrimidine and -triazine derivatives with the same qualitative activity/properties as those described in D1. This variation can, however, not be considered as inventive in view of D2 and D3. Both documents disclose also structurally related CRF antagonists. On the one hand, D2 teaches that the presence and position of nitrogen atoms in the five-membered ring is less critical

for the alleged activity. The structural unit D is equivalent to the present C-atom carrying the carbamoyl group. In D2, D may be CR4 wherein R4 inter alia denotes a COOR substituent which is already closely related to the present carbamoyl group. D3 carries at the equivalent position the group R4 which explicitly may be a carbamoyl group (see Claim 1, R4=amido). Thus, in view of D2 and D3, a skilled person would have arrived at the present compounds without any inventive ingenuity and with the expectation to provide CRF receptor antagonists when inserting a carbamoyl group in 6-position of the D1 compounds. An inventive step may, however, be recognised if the Applicant is able to show any unexpected or surprising effect over the closest prior art D1. In the absence of comparative test results or other appropriate information it is not possible to decide whether such a problem has been solved or not. In the case where comparative tests are envisaged in order to support an inventive step, these must be carried out between the compounds of the present application having the maximum structural similarity with the compounds of the closest prior art, such that the effect is shown to have its origins in the distinguishing feature of the claimed invention.

4. INDUSTRIAL APPLICABILITY

No objection.